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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT :	Christof Westenfelder	CONFIRMATION NO. :	6531
SERIAL NUMBER:	10/551,317	EXAMINER:	WEHBE, Anne Marie Sabrina
FILING DATE :	August 21, 2006	ART UNIT :	1633
FOR :	Stem-cell, precursor cell, or target cell-based treatment of multiorgan failure and renal dysfunction		

MAIL STOP AF
Commissioner for Patents
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DECLARATION OF ROBERT BRENNER UNDER 37 C.F.R. §1.132

I, Robert Brenner, of 25 Corporate Drive, Suite 360, Burlington, MA 01803, declare and state that:

1. I received my B.A. from Johns Hopkins University and my M.D. from Albert Einstein College of Medicine. I completed my medical residency in internal medicine at Brigham and Women's Hospital in Boston and my fellowship in nephrology at Stanford University Medical Center. I was Senior Vice President of Medical Affairs at AMAG Pharmaceuticals and was responsible for the company's nephrology clinical development activities. Previously, I was at Amgen for nine years where I served in a variety of nephrology leadership roles both in clinical development and medical affairs, ultimately holding the title of Executive Director and Renal Anemia Global Program Area Leader. I have contributed to the approval of new products, led the design of clinical trials, and was a key liaison to the nephrology community, professional societies and regulatory agencies. Currently, I am President and Chief Executive Officer of Allocure, Inc., which has licensed this application.

2. I have reviewed the Office action mailed on November 19, 2010. In particular I have reviewed the rejection of claims 1, 2, 6-10, 49-50 and 60 under 35 U.S.C. § 102(a) for

being anticipated by Imai *et al.* Ped. Nephrol. 17:790-794 (2002) ("Imai"). I have also reviewed the disclosure of Imai.

3. Imai does not teach the treatment of acute kidney dysfunction. Imai teaches an anti-Thy 1 antibody mediated glomerulonephritis (Thy 1 nephritis), a self-limiting disease to explore the involvement of bone marrow derived cells in glomerular remodeling.[1/] Thy 1 nephritis is a model of antibody-mediated glomerular disease.[2/] As the authors recognize, in Thy 1 nephritis normal mesangial cells (mesangial cells are macrophage like cells that are only found within the glomerulus) are disrupted (mesangiolysis), followed by an increase in the number of glomerular cells and subsequent glomerular remodeling.[3/]

4. Importantly, Thy 1 nephritis is not a model of classic acute kidney injury. Ischemia reperfusion injury is a completely different model of kidney injury. Renal artery clamping results in initial ischemia (an oxygen deprived state). Subsequent release of the renal artery clamp enables reperfusion of the ischemic kidney. Ischemia-reperfusion of this sort is a classic model of renal tubular cell injury. It is the renal tubular cells that are the most susceptible to ischemic injury, as these cells normally live in a low oxygen environment. When the kidney is challenged by low oxygen tension, as is the case with renal artery clamping, it is the tubular cells that suffer the burden of injury. This is often referred to as acute tubular necrosis, or ATN. The initial tubular injury results in altered nephron architecture, obstruction, and reduced clearance. Importantly, ischemia reperfusion injury is not a form of primary glomerular cell injury, as is the case with the Thy 1 nephritis model. Similarly, the Thy 1 nephritis model does not directly involve the renal tubular cells, and this model is not characterized by obstruction and disturbed nephron architecture.

1/ *See* Imai at page 792.
2/ *Id.* at left column.
3/ *Id.*

5. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that willful false statements may jeopardize the validity of this application and any patent issuing therefrom.

Robert Brenner

Signed this April 19 2011

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